The section entitled "Brief Description of the Drawings", which commences on page 5 of the application and ends on page 7 thereof, has been replaced with the following re-written section.

--Brief Description of the Drawings

Figure 1 is a diagrammatic representation of a single-chain binding polypeptide of the present invention. Part (a) is the extended polypeptide format and Part (b) is the folded protein format;

Figure 2 is a diagrammatic representation of a single-chain binding polypeptide of the present invention illustrating the location of the complementarity determining regions, the polypeptide spacer regions, and the effector regions;

Figure 3 is the amino acid sequence for C6.5 sFv [SEQ. ID NO. 34];

Figure 4 is the nucleotide sequence for C6.5 sFv [SEQ. ID NO 35];

Figure 5 is the amino acid sequence for C6ML3-9 sFv' [SEQ. ID NO. 36];

Figure 6 is the nucleotide sequence for C6ML3-9 sFv' [SEQ. ID NO. 37];

Figure 7 is the amino acid sequence for C6ML3-9 sFv'-L1-KDEL [SEQ. ID NO. 38];

Figure 8 is the nucleotide sequence for C6ML3-9 sFv'-L1-KDEL [SEQ. ID NO. 39];

Figure 9 is the amino acid sequence for C6ML3-9 sFv'-L2-KDEL [SEQ. ID NO. 40];

Figure 10 is the nucleotide sequence for C6ML3-9 sFv'-L2-KDEL [SEQ. ID NO. 41];

Figure 11 is the amino acid sequence for C6ML3-9 sFv'-L2-H14 [SEQ. ID NO. 42];

Figure 12 is the nucleotide sequence for C6ML3-9 sFv'-L2-H14 [SEQ. ID NO. 43];

Figure 13 is the amino acid sequence for C6ML3-9 sFv'-L2-nls [SEQ. ID NO. 44] (nls is the SV40 large T antigen nuclear localization signal);

Figure 14 is the nucleotide sequence for C6ML3-9 sFv'-L2-nls [SEQ. ID NO. 45];

Figure 15 shows that C6ML3-9 sFv' and its conjugate to salmon protamine (SP) bind specifically to erbB-2 positive ovarian cancer cells;

Figure 16 shows a FACS analysis of the erbB-2 binding activities of bacterially expressed C6ML3-9 sFv' and its derivatives;

Figure 17 is a gel shift analysis of C6.5 sFv'-SP-DNA and C6ML3-9 sFv'-SP-DNA complexes;

Figure 18 shows a kinetic study of C6.5 sFv'-SP-DNA and C6ML3-9-SP-DNA complex formation;

Figure 19 shows that a C6ML3-9 sFv-SP conjugate protein mediates specific luciferase gene delivery to erbB-2 positive cancer cells;

Figure 20 illustrates chloroquine-dependence of C6ML3-9 sFv'-SP-mediated gene delivery;

Figure 21 illustrates fluorescent microscopy of C6.5 sFv'-SP and C6ML3-9 sFv'-SP-mediated gene transfer of pGeneGrip Rhodamine/GFP plasmids with SK-OV-3 and MCF-7;

Figure 22 illustrates the effect of chloroquine on 3T3-HER2 transfection mediated by C6ML3-9 sFv'-salmon protamine;

Figure 23 illustrates the effect of chloroquine on 3T3-HER2 transfection mediated by C6ML3-9 sFv'-P1;

Figure 24 illustrates the effect of chloroquine on 3T3-HER2 transfection mediated by C6ML3-9 sFv'-H1;

Figure 25 illustrates the effect of C6ML3-9 sFv'-H1-pBks on 3T3-HER2 transfection mediated by C6ML3-9 sFv'-H1; and

Figure 26 illustrates the effect of the DNA to C6ML3-9 sFv'-H1 ratio on 3T3-HER2 transfection efficiency.--

The paragraph commencing on page 13, line 20, has been replaced with the following re-written paragraph.

--Effector sequences that facilitate coupling may comprise a segment having amino acids which may couple with or are capable of being enzymatically modified so as to be able to couple the effector segment to a nucleic-acid binding moiety. For instance, glycosylation of an engineerred Asp-X-Ser sequence results in addition of a glycosyl residue suitable for chemical coupling. Preferably, effector sequences comprise a peptide sequence that includes a cysteinyl residue. In such embodiments the effector sequence is preferably a C-terminal sequence of at least about 5 amino acid residues including a cysteinyl residue. The single-chain binding polypeptide is conjugated directly or indirectly to a nucleic acid-binding moiety or a lipid-associating moiety via the thiol group on the cysteine residue, as described in more detail hereinbelow. The effector sequence is preferably fused to the C-terminus of the single-chain binding polypeptide via recombinant DNA techniques known in the art. The resulting fusion polypeptide is known as an sFv'. An example of fusing an effector sequence to a binding polypeptide is provided in Example 2. A preferred cysteine-containing effector sequence that facilitates crosslinking is Gly_4Cys [SEQ. ID NO. 46].--

The paragraph commencing on page 14, line 15, has been replaced with the following re-written paragraph.

--Effector sequences containing endoplasmic reticulum (ER) retention signals cause the complexed protein, in this case the gene delivery vehicle, to be targeted to the ER. The ER retention signals fused to the single-chain binding polypeptide, in particular the KDEL [SEQ. ID NO. 47] sequence, redirects the gene delivery vehicle to the ER through a KDEL-receptor-mediated retrieval mechanism (Pelham, *Annu. Rev. Cell Biol.*, 5, 1-23 (1989); Zhu et al., *J. Immunol. Methods*, 231, 207-222 (1999)). The ER targeting/retention of the complexed protein/gene delivery vehicle may facilitate its endosomal escape and nuclear entry.--

The paragraph commencing on page 14, line 23, has been replaced with the following re-written paragraph.

--Effector sequences containing subcellular localization signals, such as nuclear localization signals (nls), cause a protein to be localized in the nucleus (Nigg, *Nature*, 386:779-787 (1997)). It is believed proteins recognize the nls, bind to it, and shuttle it and the complexed protein to the nucleus. A preferred nls is the SV-40 large T-antigen nuclear localization sequence TPPKKKRKV [SEQ. ID NO. 30] (Kalderon et al., *Cell*, 39, 499-509 (1984)). An example of a vehicle of the present invention including this sequence is provided in Example 2.--

The paragraph commencing on page 15, line 20, has been replaced with the following re-written paragraph.

--Examples of useful linker sequences include the amino acid sequence $[(Gly)_4Ser]_3$ [SEQ ID NO. 48] and sequences comprising 2 or 3 repeats of $[(Ser)_4Gly]_3$ [SEQ. ID NO. 49]. Preferred spacers include the same linker units for

the region between the sFv binding domains of the binding polypeptide effector regions, as well as between the effector sequence(s), when multiple effector segments are present.--

The paragraph commencing on page 16, line 14, has been replaced with the following re-written paragraph.

--Particularly preferred nucleic acid-binding proteins include salmon protamine, human protamine, a residue 11 to residue 28 subfragment of human protamine (SRSRYYRQRQRSRRRRRR [SEQ. ID NO. 33]), human histone H1 and a residue 166 to residue 192 subfragment of human histone H1 (AKKAKSPKKAKAAKPKKAP-KSPAKAK [SEQ. ID NO. 32]).--

Table 1 on pages 28 and 29 of the application has been replaced with the following rewritten Table 1.

--TABLE 1

Tumor-Associated Antigens and Peptide Epitopes

Source	TAA	Amino Acid Sequence
Adenovirus	E1A	p234-243; SGPSNTPPEI [SEQ. ID NO. 3]

Source	TAA	Amino Acid Sequence
HPV-16	E6/E7	multiple putative epitopes
	E7	p49-57; RAHYNIVTF [SEQ. ID NO. 4]
	E7	p20-29; TDLYCYEQLN [SEQ. ID NO. 5]
	E7	p45-54; AEPDRAHYNI [SEQ. ID NO. 6]
	E7	p60-79; KCDSTLRLCVQSTHVIRTL [SEQ. ID NO. 7]
	E7	p85-94; GTLGIVCPIC [SEQ. ID NO. 8]
EBV	EBNA-2	p67-76; DTPLIPLTIF [SEQ. ID NO. 9]
	EBNA-2	p276-290; PRSPTVFYNIPPMPL [SEQ. ID NO. 10]
	EBNA-3A	p330-338; FLRGRAYGL [SEQ. ID NO. 11]
	EBNA-3C	p332-346; RGIKEHVIQNAFRKA [SEQ. ID NO. 12]
	EBNA-3C	p290-299; EENLLDFVRF [SEQ. ID NO. 13]
	EBNA-4/6	p416-424; IVTDFSVIK [SEQ. ID NO. 14]
p53	p53	p264-272; LLGRNSPEV [SEQ. ID NO. 15]

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Source	TAA	Amino Acid Sequence
$p21^{ras}$	ras	p5-17; KLVVVGARGVGKS [SEQ. ID NO. 16]
	ras	p5-16; KLVVVGAVGVGK [SEQ. ID NO. 17]
	ras	p54-69; DILDTAGLEEYSAMRD [SEQ. ID NO. 18]
	ras	p60-67; GLEEYSAM [SEQ. ID NO. 19]
HER2/*neu*	neu	p971-980; ELVSEFSRMA [SEQ. ID NO. 20]
	neu	p42-56; HLDMLRHLYQGCQVV [SEQ. ID NO. 21]
	neu	p783-797; SRLLGICLTSTVQLV [SEQ. ID NO. 22]
Human Melanoma	MAGE1	p161-169; EADPTGHSY [SEQ. ID NO. 23]
	gp100	p457-466; LLDGTATLRL [SEQ. ID NO. 24]
	gp100	p280-288; YLEPGPVTA [SEQ. ID NO. 25]
	Tyrosinase	p1-9; MLLAVLYCL [SEQ. ID NO. 26]
	Tyrosinase	p368-376; YMNGTMSQV [SEQ. ID NO. 27]
	Tyrosinase	p368-376; YMNGTMSEV [SEQ. ID NO. 28]
	MART-1/Aa	p27-47; AAGIGILTVILGVLLLIGCWY [SEQ. ID NO. 29]

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The paragraph commencing at page 30, line 23, has been replaced with the following rewritten paragraph.

--The following is a description for the construction of a single-chain binding protein based on C6ML3-9 sFv but this method may be used to convert C6.5 or any other suitable single-chain sFv into a single-chain binding protein suitable for use in the present invention. To convert C6ML3-9 sFv into C6ML3-9 sFv', an oligonucleotide encoding the amino acid sequence His_6Gly_4Cys [SEQ. ID NO. 50] followed by a stop codon was fused in frame at the C-terminus of C6ML3-9 sFv using a NotI site.--

The paragraph commencing at page 31, line 6, has been replaced with the following rewritten paragraph.

--The NcoI/NotI DNA fragment encoding C6ML3-9 sFv was excised out of a plasmid vector containing the sequence and inserted into the NcoI/NotI sites of a modified pET22-b(+) from Novagen. The pET22-b was modified by insertion of an oligonucleotide encoding the amino acid sequence His_6Gly_4Cys [SEQ ID NO. 50] between the NotI and XhoI sites of the plasmids. The finished construct was named pETC6ML3-9 sFv'.--

The paragraph commencing at page 32, line 4, has been replaced with the following rewritten paragraph.

--Pel B is a secretion signal which directs the sFv' into the periplasm of bacterial cells. The spacer L1 or L2 serves as a linker between sFv' and the effector sequence, which makes the effector sequence available after the sFv' is coupled to a nucleic acid binding moiety, in particular salmon protamine, or lipid-associating moiety. The effector sequences include:

(1) SEKDEL [SEQ. ID NO. 51], an ER retention signal (Monro, S. and Pelham, H.R.B., *Cell*, 48:899-907, 1987), which had shown ER association in the absence of a typical leader sequence;

(2) the SV40 large T-antigen nuclear localization signal: TPPKKKRKV [SEQ. ID NO. 30] (Kalderon et al., *Cell*, 39:499-509 (1984)); and

(3) the amino acids 147-160 of human histone H1: KKSAKKTPKKAKKP [SEQ. ID NO. 31]; the C6ML3-9 sFv' conjugated to a related histone peptide was shown previously to mediate low levels of luciferase gene transfer without chloroquine. Chloroquine tends to accumulate into the acidic compartments of the endocytic pathway. It increases their pH, induces their swelling and eventually their leakage. This may reduce lysosomal degradation and facilitate endosomal escape.--

The paragraph commencing at page 40, line 17, has been replaced with the following rewritten paragraph.

--An H1 peptide, comprising residues 166 to 192 of human histone H1 (AKKAKSPKKAKAAKPKKAPKSPAKAK) [SEQ. ID NO. 2] was synthesized by solid phase synthesis and coupled to maleimide on its terminal amino group. C6ML3-9 sFv', at a concentration of 5-15 mg/ml^{-1}, and bearing one free SH per protein, was reacted with a ten-fold molar excess of maleimide-H1. this reaction was performed under gentle stirring for 2 hours at room temperature, protected from light, and in 100 mM phosphate buffer pH 7.4. Excess H1 peptide was removed from the reaction mix by ultrafiltration on 10 kDa polyethersulfone membrane (Pall Filtron).--

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The paragraph commencing at page 41, line 3, has been replaced with the following re-written paragraph.

--The C6ML3-9-P1 conjugate was synthesized and purified similarly using maleimide-P1 as starting material. The P1 synthetic peptide, consisting in the residues 11 to 28 of the human protamine (SRSRYYRQRQRSRRRRRR) [SEQ ID NO. 1] was synthesized by solid phase synthesis and coupled to maleimide on its terminal amino group.--

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